

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

VAN SOMEREN, Petronella,
Francisca, Hendrika, Maria
Arnold & Siedsma
Sweelinckplein 1
NL-2517 GK The Hague
PAYS-BAS

Date of mailing (day/month/year) 27 April 1999 (27.04.99)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference L/TQ04/2	
International application No. PCT/EP98/06183	International filing date (day/month/year) 25 September 1998 (25.09.98)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address	State of Nationality NL	State of Residence NL
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input checked="" type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input checked="" type="checkbox"/> the nationality <input checked="" type="checkbox"/> the residence
Name and Address UNIVERSITEIT TWENTE Drienerlolaan 5 NL-7522 NB Enschede Netherlands	State of Nationality NL	State of Residence NL
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary: The above-mentioned applicant should be included on the records as an additional applicant for all designated States except the United States of America.		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input checked="" type="checkbox"/> the designated Offices concerned	
<input checked="" type="checkbox"/> the International Searching Authority	<input type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Dominique DELMAS
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 29 June 1999 (29.06.99)	
International application No. PCT/EP98/06183	Applicant's or agent's file reference L/TQ04/2
International filing date (day/month/year) 25 September 1998 (25.09.98)	Priority date (day/month/year) 25 September 1997 (25.09.97)
Applicant KRIJGSVELD, Jeroen et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
22 April 1999 (22.04.99)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

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PATENT COOPERATION TREATY

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REC'D 10 JAN 2000

WIPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4/TQ04/cst/2	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP98/06183	International filing date (day/month/year) 25/09/1998	Priority date (day/month/year) 25/09/1997
International Patent Classification (IPC) or national classification and IPC C07K14/52		
Applicant ACADEMISCH ZIEKENHUIS BIJ DE UNIVERSITEIT .. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 22/04/1999	Date of completion of this report 29. 12. 99
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Huber, A Telephone No. +49 89 2399 8173 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP98/06183

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-19 as originally filed

Claims, No.:

1-21 as received on 06/12/1999 with letter of 06/12/1999

Drawings, sheets:

1-13 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 1, 2 (N, IS, IA), 14, 15, 19, 20 (IA).

because:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP98/06183

- ☒ the said international application, or the said claims Nos. 14, 15, 19, 20 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1, 2.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. .

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP98/06183

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10, 21
	No:	Claims	3-9, 11, 13, 14, 16, 18, 19
Inventive step (IS)	Yes:	Claims	10, 21
	No:	Claims	12, 15, 17, 20
Industrial applicability (IA)	Yes:	Claims	3-13, 16-18, 21
	No:	Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP98/06183

SECTION III

Claims 14, 15, 19 and 20 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

For the assessment of the present claims 14, 15, 19 and 20 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION IV

Independent Claim 21 is generally directed to the use of a Histag sequence for the preparation of antimicrobial peptides having an enhanced antimicrobial activity. Any antimicrobial peptide is covered by the claim, i.e. not only those of the preceding claims which all relate to antimicrobial peptides derived from thrombin-stimulated platelets. The use of Histags in general has been known in art. Also antimicrobial peptides are amply known.

Therefore, there is no common novel and inventive concept which might link the subject-matter of Claim 20 with that of Claims 1-19.

Since no objection to lack of unity of invention has been raised by the search authority, the IPEA decided not to raise an objection during preliminary examination. However, this objection will be prosecuted during regional phase examination at the EPO.

SECTION V

1. The present application relates to microbicidal peptides which are released from thrombin-activated platelets. The peptides are termed thrombocidin 1 (TC-1) and

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP98/06183

thrombocidin-2 (TC-2). Further included are variants of said peptides. The peptides are useful in the treatment and prevention of bacterial and fungal infections such as endocarditis.

2. Reference is made to the following documents:

D1: WO - A - 90/06321

D2: WO - A - 97/19173

D3: S.A.J. ZAAT ET AL.: 'Cell-Adherent Glucan does not Protect Endocarditis-Causing Viridans Streptococci Against Bactericidal Proteins from Human Blood Platelets' ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, vol. 418, 1997, XP002099203

D4: J. DANKERT ET AL.: 'Involvement of Bactericidal Factors from Thrombin-Stimulated Platelets in Clearance of Adherent Viridans Streptococci in Experimental Infective Endocarditis' INFECTION AND IMMUNITY, vol. 63, no. 2, February 1995, pages 663-671, XP002099202 WASHINGTON US

D5: M.R. YEAMAN ET AL.: 'Partial Characterization and Staphylocidal Activity of Thrombin-induced Platelet Microbicidal Protein' INFECTION AND IMMUNITY, vol. 60, no. 3, March 1992, pages 1202-1209, XP002099201 WASHINGTON US

D6: M.R. YEAMAN ET AL.: 'Platelet Microbicidal Protein alone and in Combination with Antibiotics Reduces Staphylococcus aureus Adherence to Platelets In Vitro' INFECTION AND IMMUNITY, vol. 62, no. 8, August 1994, pages 3416-3423, XP002099200 WASHINGTON US

3. No search report has been established for Claims 1 and 2 (former Claim 1). Therefore, no preliminary examination of these claims can be carried out. It should, however, be noted that microbicidal peptides having a specific arrangement of four cysteine residues are known from the prior art (see e.g. D1

and D2).

4. In the amended set of claims the term "antimicrobial" has been replaced by the term "microbicidal". Both expressions can be used synonymously and mean that the peptides have activity against microorganisms.

The argument of the applicant that the claimed peptides are distinguished from prior art peptides in that it has surprisingly been found that the platelet-derived chemokines and thrombocidins have a direct microbicidal activity, i.e. that the peptides act by direct interaction with the microorganisms is not shared by the IPEA.

Firstly, it should be noted that said feature is not reflected in the claims. Moreover, the mode of action does not render already known proteins novel. It is irrelevant for the novelty of a microbicidal protein whether the microbicidal activity of the peptide is exhibited directly or indirectly through the activation of leukocytes. . The subject-matter of Claims 3-9, 11, 13, 14, 16, 18 and 19 is therefore not novel in view of the prior art as detailed below (Art. 33(2) PCT).

- 4.1 Claim 3 relates to microbicidal peptides which are CXC chemokines. Antimicrobial peptides belonging to the CXC family are known from the prior art, see e.g. D1 (NAP-2) and D2 (KC, gro- α , gro- β , and gro- γ) which disclose chemokines having the specific arrangement and disulfide-linkage of four cysteine residues which is typical for the CXC family.

Hence, the subject-matter of Claim 3 is not novel with regard to any of these documents (Art. 33(2) PCT).

- 4.2 Claims 4 and 5 are directed to microbicidal peptides which are characterized by their name (thrombocidin-1, thrombocidin-2) and to variants thereof comprising at least in part the sequence of TC-1 and TC-2 shown in Fig. 1a.

First of all it should be noted that the definition of an - allegedly - novel protein merely by a name is not sufficient to allow the unambiguous identification of the claimed protein. A protein should be defined in the claims by technical features such as its amino acid sequence.

In addition, the amino acid sequence is an inherent property of a protein. Thus, a protein which has been known before but its amino acid sequence had not yet been determined, is not rendered novel when its amino acid sequence is

elucidated. Partially purified thrombocidin and its bactericidal activity is described in D3. The bactericidal factor described in D4 also appears to be thrombocidin. The factor is released from thrombin activated platelets (see also reference 3 in D3).

The same applies to the thrombin-induced platelet microbicidal protein PMP described in D5. The factor has been partially purified and has an apparent molecular weight of 8.5 kDa on SDS-PAGE.

PMP was shown to reduce the bacterial adherence to platelets and it is suggested that the factor may play an important role in defense against infective endocarditis (see D6).

- 4.3 Moreover, the amino acid sequence of TC-1 shown in Fig. 1 is almost identical to that of NAP-2 (see D1, Fig. 4), only the two N-terminal amino acids are absent. NAP-2 can therefore be regarded as a variant of TC-1 which comprises at least in part the sequence of TC-1. NAP-2 is indicated for the treatment of infectious diseases caused by bacteria, viruses or fungi (see D1, page 9, third paragraph). In Fig. 5 of D1 also the amino acid sequence of CTAP-III is shown, which is identical to TC-2 except for the last two amino acids. CTAP-III therefore comprises the amino acid sequence of TC-2 and thus falls under the scope of Claim 5. Also the antimicrobial peptides of D2 can be considered as variants of TC-1 and TC-2. They share extensive amino acid homology with TC-1 and TC-2 and comprise, in part, the sequences shown in Fig. 1. They exhibit antibacterial activity against gram-negative bacteria, such as E.coli and also against some gram-positive bacteria such as Staphylococcus.
- The subject-matter of Claims 3-9, 11, 13, 14, 16, 18 and 19 is therefore not novel with regard to D1 or D2 (Art. 33(2) PCT).
5. Thrombin-induced antimicrobial factors have already been proposed for the treatment of endocarditis (see D3, D4 and D6). Therefore, no inventive step can be acknowledged for the subject-matter of Claims 12, 15, 17 and 20 (Art. 33(3) PCT).

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference L/TQ04/2	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 98/ 06183	International filing date (day/month/year) 25/09/1998	(Earliest) Priority Date (day/month/year) 25/09/1997
Applicant ACADEMISCH ZIEKENHUIS BIJ DE UNIVERSITEIT . . et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 98/06183

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: As far as claims 13,14,18 and 19
are directed to a method of treatment of the human/animal
body, the search has been carried out and based on the alleged
effects of the compound/composition.
2. ☒ Claims Nos.: 1
because they relate to parts of the International Application that do not comply with the prescribed requirements to such
an extent that no meaningful International Search can be carried out, specifically:
See FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: 1

Claims 1 is directed to peptides which 'have a three-dimensional structure as shown in figure 13'. Figure 13 is a very raw sketch which provides nearly to no hints about the three dimensional structure of a protein. Even if there was a proper picture of three dimensional structure given, it would have been impossible to conduct a search for proteins having the same structure. The ISA simply does not have the means to conduct searches on compounds based on their three dimensional structure.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/06183

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07K14/52 A61K38/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M.R. YEAMAN ET AL.: "Platelet Microbicidal Protein alone and in Combination with Antibiotics Reduces Staphylococcus aureus Adherence to Platelets In Vitro" INFECTION AND IMMUNITY, vol. 62, no. 8, August 1994, pages 3416-3423, XP002099200 WASHINGTON US see page 3416, right-hand column, paragraph 2 see page 3420, right-hand column, last paragraph - page 3421, right-hand column, last paragraph --- -/--	3,4,6-8, 10-13, 15,17,18

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

8 April 1999

Date of mailing of the international search report

22/04/1999

Name and mailing address of the ISA

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Authorized officer

Fuhr, C

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	M.R. YEAMAN ET AL.: "Partial Characterization and Staphylocidal Activity of Thrombin-induced Platelet Microbicidal Protein" INFECTION AND IMMUNITY, vol. 60, no. 3, March 1992, pages 1202-1209, XP002099201 WASHINGTON US see page 1207, left-hand column, last paragraph - page 1208, right-hand column, paragraph 2 ---	3,4,6-8, 10-13, 15,17-19
X	J. DANKERT ET AL.: "Involvement of Bactericidal Factors from Thrombin-Stimulated Platelets in Clearance of Adherent Viridans Streptococci in Experimental Infective Endocarditis" INFECTION AND IMMUNITY, vol. 63, no. 2, February 1995, pages 663-671, XP002099202 WASHINGTON US see page 665, left-hand column, last paragraph - right-hand column, paragraph 2 see page 669, left-hand column, paragraph 2 - page 670, right-hand column, paragraph 3 ---	3,4,6-8, 10-13, 15,17-19
X	S.A.J. ZAAT ET AL.: "Cell-Adherent Glucan does not Protect Endocarditis-Causing Viridans Streptococci Against Bactericidal Proteins from Human Blood Platelets" ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, vol. 418, 1997, XP002099203 see page 710, paragraph 2 - paragraph 4 ---	3,4,6-8, 10-13, 15,17-19
X	T.J. STANDIFORD ET AL.: "Role of Chemokines in Antibacterial Host Defense" METHODS IN ENZYMOLOGY, vol. 288, 1997, pages 220-241, XP002099204 see page 224 - page 225 ---	1,2
X	HARWIG S S L: "PURIFICATION OF CYSTEINE-RICH BIOACTIVE PEPTIDES FROM LEUKOCYTES BY CONTINUOUS ACID-UREA-POLYACRYLAMIDE GEL ELECTROPHORESIS" ANALYTICAL BIOCHEMISTRY, vol. 208, no. 2, 1 February 1993, pages 382-386, XP000335009 see the whole document --- -/--	1-3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/06183

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 19173 A (SMITHKLINE BEECHAM CORP ; DEMARSH PETER LAWRENCE (US); JOHANSON KYU) 29 May 1997 see page 3, line 11 - line 20 see page 4; claims; examples ---	1,2,5,6, 8,10-13
X	WO 90 06321 A (KOCHER THEODOR INST ; SANDOZ AG (CH)) 14 June 1990 see page 9, paragraph 3; claims; examples ---	1,2,5,6, 8,10-19
X	DATABASE MEDLINE US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US YEAMAN M R ET AL: "Fluconazole and platelet microbicidal protein inhibit Candida adherence to platelets in vitro." XP002099205 see abstract & ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1994 JUL) 38 (7) 1460-5. JOURNAL CODE: 6HK. ISSN: 0066-4804., United States ---	3,4,7, 15,17,18
X	DATABASE MEDLINE US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US YEAMAN M R ET AL: "Thrombin-induced rabbit platelet microbicidal protein is fungicidal in vitro." XP002099206 see abstract & ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1993 MAR) 37 (3) 546-53. JOURNAL CODE: 6HK. ISSN: 0066-4804., United States -----	3,4,7, 15,17,18

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 98/06183

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9719173	A	29-05-1997	AU	1020997 A	11-06-1997
			EP	0871732 A	21-10-1998
<hr/>					
WO 9006321	A	14-06-1990	AU	634508 B	25-02-1993
			AU	4655689 A	26-06-1990
			BE	1003636 A	12-05-1992
			CA	2004685 A	08-06-1990
			CH	681625 A	30-04-1993
			DK	188690 A	07-08-1990
			ES	2047458 A	16-02-1994
			FR	2640142 A	15-06-1990
			GB	2231872 A, B	28-11-1990
			GR	89100810 A, B	15-03-1991
			IT	1238229 B	12-07-1993
			JP	3503767 T	22-08-1991
			NL	8921262 A	01-11-1990
			PT	92509 A	29-06-1990
			SE	9002589 A	07-08-1990
			US	5759533 A	02-06-1998
<hr/>					